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MULTIPLE EVENT ANALYSIS OF INJURIES USING ADAPTATIONS TO THE COX PROPORTIONAL HAZARDS MODEL

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Understanding the epidemiology of injuries is of great importance to the United States Military. However, there is presently limited information regarding statistical methodology, as it pertains to a setting where an individual can experience multiple injuries. This thesis explores the use of three statistical models, each with distinctive underlying assumptions, that are commonly used in recurrent failure time settings. Each was applied to the same data set of United States Army Airborne soldiers (n=1214). The outcome of interest was lower extremity or low back injury, and only the first and second injury events were examined. The methods employed were two Cox Proportional Hazards Models, each representing a separate injury event; the Andersen-Gill (AG) Multiplicative Hazards Model, which employs a counting process formulation; and the Prentice, Williams and Petersen (PWP) Model, where the multiple events are modelled via stratification. The final results for the Cox Model to first injury, and the first strata of the PWP Model are equivalent. The final AG Model, yielded coinciding covariates to the first injury event in the other models, with minimal differences between the parameter estimates. Similarly, the final Cox Model for the second injury event and the second strata of the PWP Model are equivalent; however, they produce different risk factors than the Cox Model for first event and the first strata of the PWP Model. The comparison of the different methodologies demonstrate that the PWP Model is best suited for the multiple injury setting. The facts that both the baseline hazard and the parameter estimates alter by event, and that it allows for easy comparison between strata (injury events), justifies this claim.

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MULTIPLE EVENT ANALYSIS OF INJURIES USING ADAPTATIONS TO THE COX PROPORTIONAL HAZARDS MODEL

A Thesis Presented

by

GARY A. SCHNEIDER

Submitted to the Graduate School of the
University of Massachusetts Amherst in partial fulfillment
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DEDICATION

To the memory of my grandfather, Seymour Samuels, whose unparalleled support, motivation, and non-judgmental attitude has and will continue to be of the utmost influence in all of my accomplishments, no matter how large or small.

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ABSTRACT

MULTIPLE EVENT ANALYSIS OF INJURIES USING ADAPTATIONS
TO THE COX PROPORTIONAL HAZARDS MODEL

SEPTEMBER 1997

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Understanding the epidemiology of injuries is of great importance to the United States Military. However, there is presently limited information regarding statistical methodology, as it pertains to a setting where an individual can experience multiple injuries. This thesis explores the use of three statistical models, each with distinctive underlying assumptions, that are commonly used in recurrent failure time settings. Each was applied to the same data set of United States Army Airborne soldiers (n=1214). The outcome of interest was lower extremity or low back injury, and only the first and second injury events were examined. The methods employed were two Cox Proportional Hazards Models, each representing a separate injury event; the Andersen-Gill (AG) Multiplicative Hazards Model, which employs a counting process formulation; and the Prentice, Williams, and Peterson (PWP) Model, where the multiple events are modelled via stratification.

The final results for the Cox Model to first injury, and the first strata of the PWP Model are equivalent. The final AG Model, yielded coinciding covariates to the first injury event in the other models, with minimal differences between the parameter estimates. Similarly, the final Cox Model for the second injury event and the second strata of the PWP Model are equivalent; however, they produce different risk factors than the Cox Model for first event and the first strata of the PWP Model.

The comparison of the different methodologies demonstrate that the PWP Model is best suited for the multiple injury setting. The facts that both the baseline hazard and the parameter estimates alter by event, and that it allows for easy comparison between strata (injury events), justifies this claim.

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CHAPTER 1

INTRODUCTION

Individuals in the military, by virtue of their occupation and demographic profile, are at high risk for injury. The reduction in productivity and economic effects of injury are profound: however, there is limited understanding regarding associated risk factors. A recent effort by the Armed Forces Epidemiology Board culminated in the publication of Injuries in the Military - A Hidden Epidemic. This report provides a comprehensive review of the extent of the injury problem for the United States Military (Jones and Hanson, 1996). Within this report it is suggested that "previous injury history" and the "late effects of injury" have an effect on subsequent risk of injury. These conclusions resulted from review of hospitalization data and results from epidemiologic risk factor studies in which previous injury history was determined by self report. Additionally, the two cited epidemiological studies in which previous injury history was examined have contradictory findings. One suggests that previous injury history is a risk factor for later injury (Jones et al., 1993). The other suggests a protective effect (Brodine and Shaffer, 1995). Such disagreement suggests further inquiry concerning the effect of previous injury on subsequent injury is needed. Increasing the understanding regarding the effect of previous injury history is therefore one of the objectives of this thesis.

The most comprehensive way to examine previous injury history as a potential risk factor for injury would be to prospectively follow a cohort of individuals for a time interval of adequate duration so that there would be a subgroup of subjects who experienced two or more injuries. Comprehensive collection of all injury data should be extracted from the individual's medical record in order to ensure maximum ascertainment of injury events. There have been no published risk factor studies conducted on military populations in which previous injury history was determined from the individual's medical records.

Prospective examination of the population would provide many benefits. Both type and severity of previous injury could be evaluated, as well as multiple aspects of the medical care provided. These possible risk factors can be examined concurrently with previously identified risk factors. Additionally, the effect of elapsed time since previous injury on subsequent injury can be explored.

Unfortunately, the statistical tools needed for the proper analysis of recurrent injury data require sophisticated techniques that are largely untested for this purpose. This is primarily because the addition of the medical record review to assess previous injury history necessitates the study of a dynamic cohort of individuals, some of which may not have an injury during the study interval. This analysis is further complicated by the multiple injury setting. Therefore an additional focus of this thesis is to examine different analytical approaches to model risk factors for injury in a recurrent event setting.

CHAPTER 2

REVIEW OF THE LITERATURE

Preface

In order to understand the intricacies of fitting different regression models to recurrent injury data in military populations, the extent of the injury problem in the military should first be examined. The first section of the literature review provides the reader with an appreciation of the magnitude of this problem while providing a sense of the extent of the surveillance and epidemiologic investigation that has been used to examine injury in the military.

This is followed by a comprehensive explanation of the Cox Proportional Hazards Model, which is often used for survival analysis in epidemiologic studies. An adaption of this model will be one of the three used for the analyses conducted for this thesis. Specifically, in this analysis, two separate Cox models will be fit. The first will include the entire cohort and will model time to first injury. The second will include only those individuals who had an event of interest in the first model and will model time from first injury to second injury.

The final section of this literature review will focus on the Anderson-Gill Multiplicative Hazard (AG) Model, and the Prentice, Williams and Peterson (PWP) Model. These techniques permit the modelling of multiple events per individual within one regression model. The mechanisms used are a counting process and a stratification

approach in the AG model and PWP model, respectively. In both cases these models reduce to the single event Cox model in the absence of multiple events.

Section 1 - Injury in the Military

Background

Until recently the extent of the problem of physical injuries in the United States Military was not widely appreciated. However, in 1994, at the request of the Office of the Surgeon General of the Army, the Armed Forces Epidemiology Board formed the Injury Prevention and Control Work Group. The primary objectives of this work group were to determine how large a problem personal injury in the military is, what information/databases currently exist that can be used to explore this problem and to develop strategies to prevent injuries. This work led to the publication of a report entitled, "Injuries in the Military - A Hidden Epidemic," in November 1996. Personal injury can vary in severity. Recognizing this, the Injury Prevention and Control Work Group examined the problem of injury in four primary categories: nonhostile casualties, disabilities, hospitalizations, and outpatient visits. The following section of this literature review is a synopsis of only the segments of this report describing the magnitude of the problem of personal injury in the military in each of these four categories.

Nonhostile Casualties

During the time interval from 1980 to 1992, the leading cause of nonhostile (not battle related) casualties in the U.S. Army was physical injury, accounting for 80% of these deaths. The incidence rate for these "injury related deaths" was approximately 80 individuals per 100,000 person years. The mechanisms for injury were accidents, suicide, and homicide which were responsible for 62%, 12% and 6% of all nonhostile casualties, respectively. Illness was the cause of the remaining 20% of nonhostile casualties. This clearly demonstrates that physical injury, regardless of the mechanism, is the most prominent cause of non-battle related deaths in the Army.

Disabilities

The extent of the problem of injuries resulting in disability can be best described by its economic impact. All disability claims are reviewed by a Physical Evaluation Board (PEB) charged with determining an individuals fitness for continued service. These decisions are based on input from medical evaluation boards and line of duty determination reports. The lifetime cost of all new disability claims awarded by Army PEBs in 1993 is estimated to be 485 million dollars. The annual cost to the government for individuals receiving either permanent or temporary disability is immense. In 1990 the cost of disability to the Department of Defense was nearly 1.5 billion dollars. However, individuals often collect disability claims from the Veterans

Administration. This agency has an annual cost of approximately 12 billion dollars for disability claims (Amoroso, 1997).

Medical complaints associated with musculoskeletal injury constituted the five leading reasons for disability cases reviewed by Army PEBs in 1994. This accounted for 16.7% of all disability claims for this year. Between 1989 and 1993 the Navy conducted approximately 75,000 PEBs, of these 22,125 (29.5%) had ICD-9 codes that corresponded to either musculoskeletal or injury categories, both of which are likely to be the result of injury.

Hospitalizations

The lifetime cost of all injuries resulting in hospitalization during 1985 for the entire United States population is estimated at 80.1 billion dollars. The age group that is responsible for the largest fraction of this cost is the 15-44 year old group. This cost of injuries in this age group is approximately twice that of fatal injuries and three times that of non-hospitalized injuries. While similar data do not currently exist for the military, the majority of the military is in the 15-44 year old bracket: thus hospitalized injuries are considered to be a major medical problem in the military.

Desert Storm data suggest that unintentional injury, other acute injuries and other musculoskeletal conditions accounted for 43% of all hospitalizations during this operation; there were very few hospitalizations due to combat during Desert Storm. Approximately 14% of all hospitalizations during Desert Storm were due to

musculoskeletal and connective tissue disorders, many of which were the effects of previous injury.

The leading causes of injury that resulted in hospitalization among Army active duty personnel in 1992 were the late effects of injury and athletics/sports-related injuries. These accounted for 18% and 13.3% of the 15,365 injury-related hospitalizations that received an external cause code, respectively. There were an additional 76,423 injury-related hospitalizations to active duty Army personnel that occurred during 1992, of which the causes are unknown.

Outpatient Visits

Injuries resulting in outpatient medical visits have the largest impact on military readiness. It is estimated that in 1994 there were 400,000 injury-related outpatient visits in the Army that resulted in 1.2 million limited duty days. For comparison purposes, the estimated number of nonhostile deaths, disabilities and hospitalizations that were the result of injury in the same time interval were 350, 4,500 and 20,000, respectively (Figure 1). There is not yet a comprehensive source of data in which injuries that result in outpatient medical visits can be examined. However, the magnitude of this problem has been studied in epidemiologic studies that have primarily examined cohorts of soldiers in controlled training environments.

In one such study the extent of the problem of "outpatient injuries" was compared to "outpatient illnesses" in 124 male and 186 female Army recruits. The

number of injury visits was similar to the number of illness visits, with injury to illness ratios of 0.8 and 1.1 for males and females, respectively. Injuries, however, resulted in 5.1 times more limited duty days than illnesses for the male recruits, and 21.5 times more limited duty days in the female recruits (Jones et al. 1988). This illustrates the magnitude of the problem of outpatient injuries in terms of military readiness in comparison to other medical complaints.

Most of these studies sought to determine risk factors for injury. While there is some variation in the results of these studies, some common risk factors have been identified. The most common of these are lower level physical fitness and lower level past physical activity. Other agreed upon risk factors are younger age, and selected behaviors such as cigarette or alcohol use. Other studies suggest that high amounts of weekly exercise, high running mileage, and previous injury history effect the risk of injury.

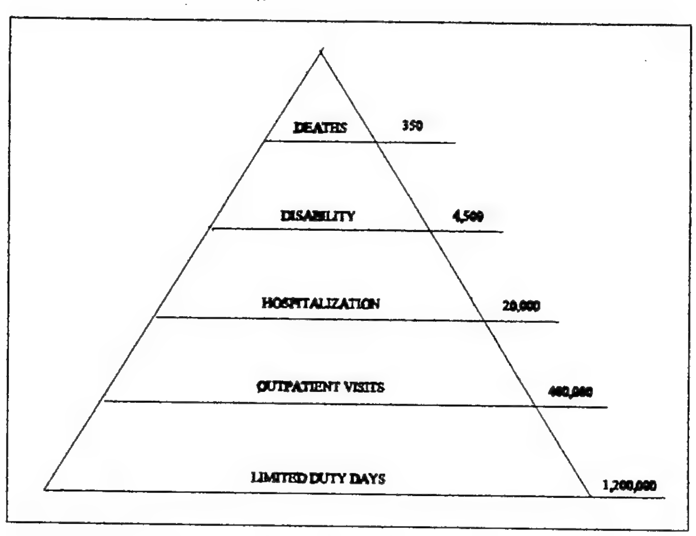

Figure 1 - The Army Injury Pyramid

Conclusion

As a result of the efforts of the Injury Control Work Group, the Armed Forces Epidemiology Board recognizes injury as the leading medical problem that effects military readiness. It recommends that numerous improvements be made in many aspects of injury surveillance and prevention efforts. This would include the establishment of a database linking hospitalization, disability and fatality data sources at a central site and the development of an outpatient surveillance system. Additionally, it recommends that these systems should be standardized and compatible between the separate military branches and with civilian surveillance systems. This would in turn improve the capabilities of injury prevention research, which is recognized as instrumental in developing an increased understanding of the causes of injury as well as improving prevention strategies.

Section 2 - Time Dependant Single Event Analysis Using the Cox Proportional Hazards Model

Derivation of the Likelihood

The unconditional full likelihood for a time dependent single event analysis represents each outcome as a triplet of the form

$$[t_i, c_i, \underline{x}_i(t_i)] \text{ where,}$$

t_i = time to last contact
c_i = event indicator (0=censored, 1=event)
$\underline{x}_i(t_i)$ = vector of explanatory variables, possibly a function of t_i

with i=1 to N indexing the subjects, assumed independent.

Consider a censored outcome at time t. All that is known about this individual is that their survival time is greater than t. Thus, his/her contribution to the unconditional full likelihood is the probability that an individual with associated covariate pattern $\underline{x}$ survives until at least time t. This is synonymous with the survivorship function, S(•). Since c=0 for a censored outcome, the contribution to the likelihood may be expressed as follows:

$$[S(t, \underline{\beta}, \underline{x}(t))]^{1-c},$$

where S(•) is the survivorship function and is assumed to be related to the vector of covariates, $\underline{x}(t)$, through an associated vector of regression coefficient $\underline{\beta}$.

Consider next an actual event occurring at time t. Here, the contribution to the likelihood is identically the density function, f(•). Thus with c=1 for an actual event, the contribution to the likelihood function becomes the following:

$$[f(t, \underline{\beta}, \underline{x}(t))]^c$$

Again, f(•) is assumed to be related to the vector of covariates, $\underline{x}(t)$, through an associated vector of regression coefficients.

For a sample of N individuals, the unconditional full likelihood is the product of the N independent contributions. Thus,

$$L(\underline{\beta}) = \prod_{i=1 \text{ to } N} [S(t, \underline{\beta}, \underline{x}(t))]^{1-c} [f(t, \underline{\beta}, \underline{x}(t))]^c$$

This unconditional full likelihood is completely general. No assumptions have been made about the form of S(•) and f(•), the link between $\underline{x}(t)$ and S(•) and f(•), nor the relationship between the event and censoring mechanisms. Thus, further assumptions and a model are needed in order to make inferences about β (Hosmer, 1996).

<u>Heuristic of the Cox Proportional Hazards Model</u>

Cox's (1972) formulation of the Proportional Hazard Model derives from a partial likelihood function that conditions on the set of actual event times and exploits two assumptions:

(1) The censoring mechanism is independent of the event mechanism.
(2) The hazard function $h(t, \underline{\beta}, \underline{x})$ is linked to the explanatory variables via the model

$$h(t, \underline{\beta}, \underline{x}) = h_o(t) \exp[\underline{x}(t)'\underline{\beta}]$$

where $h_o(t)$ is an arbitrary baseline hazard function that is independent of $\underline{x}(t)$ for all t.

The advantage to conditioning on the set of actual event times is that it avoids having to make an assumption about the form of S(•) and f(•); e.g. - exponential, Weibull, etc. The advantage to assuming that the censoring mechanism is independent of the event mechanism is that it permits analysis of a partial likelihood which considers only observed actual events and the associated risk sets.

The Cox Proportional Hazards Model and the Underlying Partial Likelihood

As indicated above, the conditional likelihood used to derive the partial likelihood that underlies the Cox Proportional Hazards Model conditions on the set of ordered occasions on which actual events occurred. Suppose there are n actual events, $n \le N$. If these are denoted using the usual order statistic notation, $\{t_{(i)}\}$, the conditional likelihood of interest is that of

$$[t_1, c_1, \underline{x}_{(1)}(t_1)], \ldots\ldots, [t_n, c_n, \underline{x}_{(n)}(t_n)] \mid \{t_{(i)}\}$$

Without loss of generality, suppose C_1 individuals are censored prior to the first event, an additional C_2 individuals are censored prior to the second event, and so forth. Arguing conditionally on the set of event times $\{t_{(i)}\}$ allows us to write the conditional likelihood as the following product:

$$L_{cond}([t_1, c_1, \underline{x}_1(t_1)], \ldots\ldots, [t_n, c_n, \underline{x}_{(n)}(t_n)] \mid \{t_{(i)}\}) =$$

$$L[C_1 \text{ censored in } (0,t_{(1)}^-), \text{ No events in } (0,t_{(1)}^-)] \bullet$$
$$L[\text{1st event at } t_{(1)} \mid \text{history to } t_{(1)}^-] \bullet \ldots\ldots \bullet$$
$$L[n^{th} \text{ event at } t_{(n)} \mid \text{history to } t_{(n)}^-] \bullet L[C_{n+1} \text{ censored after } t_{(n)}]$$

where for ease of notation, "history to $t_{(1)}^-$," is shorthand for "no events in $(0, t_{(1)}^-)$," "history to $t_{(2)}^-$," is shorthand for "no events in $(0, t_{(1)}^-)$, one event at $t_{(1)}$, no events in $t_{(1)}^+, t_{(2)}^-$)," etc. Following Andersen et al (1993, page 49), these "histories" are denoted $\mathscr{F}_t$. Thus $\mathscr{F}_t$ represents the available data at time t, and $\mathscr{F}_{t^-}$ represents the available data at time t^-. Thus, the conditional likelihood can be constructed incrementally over the occasions of censoring and event times by exploiting the theorem of total probabilities. The first term represents the likelihood of the first C_1 censorings, the second term represents the likelihood of the first event at time $t_{(1)}$, conditional on the history to time $t_{(1)}^-$, and so on. This is analogous to the lifetable approach to estimating survival probabilities. Further inspection reveals that this conditional likelihood contains two types of terms: one corresponding to the occasions of censoring and the other corresponding to occasions of the actual events. When these are regrouped, the full conditional likelihood is seen to be of the following form:

$$L_{cond}\{[t_1, c_1, \underline{x}_1(t_1)], \ldots\ldots, [t_n, c_n, \underline{x}_n(t_n)] \mid \{t_{(i)}\}\} =$$

$$\prod_{j=1 \text{ to } n} L[j^{th} \text{ event at time } t_{(j)} \mid \mathscr{F}t_{(j)}^-] \bullet \prod_{j=1 \text{ to } n} L[C_j \text{ censored in } (t_{(j-1)}^+,\ t_{(j)}^- \mid \mathscr{F}t_{(j-1)}]$$
$$\bullet\ L[C_{n+1} \text{ censored at } t_{(n)} \mid \mathscr{F}t_{(n)}]$$

Here the subscript j indexes the n actual event times and by definition, $t_{(0)}^+ = 0$.

The Cox Proportional Hazards Model partial likelihood is extracted from the conditional likelihood by dropping the censoring likelihood terms. Justification is the assumption that the censoring mechanism is independent of the event mechanism and that the censoring likelihood terms contain no information about $\underline{\beta}$. We then obtain:

$$L\{[t_1, c_1, \underline{x}_1(t_1)], \ldots\ldots, [t_N, c_N, \underline{x}_N(t_N)] \mid \{t_{(i)}\}\}_{partial} = \prod_{j=1 \text{ to } n} L[j^{th} \text{ event at time } t_{(j)} \mid \mathscr{F}t_{(j)}^-]$$

The conditional likelihood, L[j^{th} event at time $t_{(j)}$| $\mathscr{F}t_{(j)}^-$] can then be seen to be equal to the following:

$$L[j^{th} \text{ event at time } t_{(j)} | \mathscr{F}t_{(j)}^-] =$$
$$L[j^{th} \text{ event at time } t_{(j)} | j^{th} \text{ survives to time } t_{(j)}^-] \div$$
$$\sum_{u: Rj} L[u^{th} \text{ event at time } t_{(j)} | u^{th} \text{ survives to time } t_{(j)}^-]$$

where R_j is the subset remaining at risk at time $t_{(j)}^-$.

Notice that the assumption of independence of the event and censoring mechanisms permits replacing the condition " history to time $t_{(j)}^-$ " with the risk set at time $t_{(j)}^-$, which is denoted R_j. Finally, noting that L[u^{th} event at time $t_{(j)}$ | u^{th} survives to time $t_{(j)}^-$] is by definition the hazard function, yields the following partial conditional likelihood:

$$L\{[t_1, c_1, \underline{x}_1(t_1)], \ldots\ldots, [t_N, c_N, \underline{x}_N(t_N)] \mid \{t_{(i)}\}\}_{partial} =$$
$$\prod_{j=1 \text{ to } n} [h(t_{(j)}, \beta, \underline{x}_j) \div \sum_{u: Rj} h(t_{(j)}, \beta, \underline{x}_u)]$$

As in lifetable methods of estimation, censored observations are retained in the likelihood as long as they are at risk.

Finally, substitution of the Cox Proportional Hazards Model assumption yields:

$$L\{[t_1, c_1, \underline{x}_1(t_1)], \ldots\ldots, [t_n, c_n, \underline{x}_n(t_n)] \mid \{t_{(i)}\}\}_{partial} =$$
$$\prod_{j=1 \text{ to } n} \{ h_o(t_{(j)}) \exp[\underline{x}(t_{(j)})'\underline{\beta}] \div \sum_{u: Rj} h_o(t_{(j)}) \exp[\underline{u}(t_{(j)})'\underline{\beta}] \} =$$
$$\prod_{j=1 \text{ to } n} \{\exp[\underline{x}(t_{(j)})'\underline{\beta}] \div \sum_{u: Rj} \exp[\underline{u}(t_{(j)})'\underline{\beta}] \}$$

Maximum likelihood based inference for $\underline{\beta}$ is based on this function.

Section 3 - Time Dependent Multiple Event Models

The Anderson-Gill Model

The Anderson-Gill (AG) Model, often referred to as the Multiplicative Hazards Model, utilizes a counting process formulation. This framework has the advantage of simplifying the modeling of a recurrent event in the presence of censoring and of permitting straightforward application of counting process theory in the derivation of large sample properties (Andersen and Gill, 1982).

For ease of presentation, some necessary notation is defined and explained. As well, for clarity, the Cox Proportional Hazards Model is reformulated using this notation. Then, the AG Model is defined.

Let j index the individuals in the sample j=1,2,....,N. Consider first the experience of a single individual, j. Recall that, in the Cox Proportional Hazards Model, his/her conditional hazard of event at time t, $h_j(t)$, is modelled as a function of time t and a vector of explanatory variables, $x_j(t)$. Specifically,

$$h_j(t) = h_o(t) \exp [\underline{x}_j(t)'\underline{\beta}]$$

where $\underline{\beta}$ is the associated vector of regression coefficients. Let

$$Y_j(t) = I\ \{t_j \leq t\}$$

where t_j is the time to last contact, as defined previously. Thus, $Y_j(t)$ is an indicator of risk at event at time t^{-}. Define an intensity process, $\lambda_j(t)$ as follows:

$$\lambda_j(t) = Y_j(t)\ h_j(t)\ .$$

The intensity process $\lambda_j(t)$ is directly interpretable as the product of a risk indicator multiplied by the hazard of the event. Recall next that $C_j(t)$ is a censoring indicator with unity indicating occurrence of an actual event. Define next a <u>counting process</u> $N_j(t)$ which counts the number of actual events that have occurred prior to and including time t.

$$Nj(t) = \int_0^t I \{C_i(u) = 1\} du$$

The equivalence of the formulation of the Cox Proportional Hazards Model described previously and the counting process formulation exploits the following heuristic. Consider a small increment of time, $(t, t+\Delta t]$. As Δt approaches zero, the expected change in the number of events in this interval is identically the same as the expected number of events in this interval; i.e.- some number between 0 and 1. It follows that modelling the conditional intensity process is identically the same as modelling the conditional counting process. Recalling that $\mathscr{F}_{t^-}$ represents the available data at t^-, the "history to time t^-," this equivalence is given by:

$$E [N_j(t) \mid \mathscr{F}_{t-}] = \lambda_j(t)$$

Thus, the Cox Proportional Hazards Model can be equivalently formulated in the counting process framework, specifically:

$$\begin{aligned} E [N_j(t) \mid \mathscr{F}_{t-}] &= \lambda_j(t) \\ &= Y_j(t)\, h_j(t) \\ &= Y_j(t)\, h_o(t) \exp [\underline{x}_j(t)'\underline{\beta}] \end{aligned}$$

In this thesis, the AG Model that is considered is an extension of this model to the setting where a person can experience 0, 1, or 2 events. The AG model has the same definition. Specifically:

$$E\,[N_j(t) \mid \mathscr{F}_{t-}] = Y_j(t)\, h_o(t) \exp\,[\underline{x}_j(t)'\underline{\beta}]$$

The distinction between the AG Model and the Cox Proportional Hazards Model is that, in the AG model, $\mathscr{F}_{t-}$ captures possibly one or more prior events (Andersen et al., 1993).

Implicit in this AG Model are three strong assumptions:

1) multiple event times for a single individual are mutually independent;
2) the baseline hazard does not vary by event; and
3) the values of the regression parameters do not vary by event.

Let i index the n actual event times $\{t_i : i=1,2,....,n\}$. In a sample of N individuals in which there are $n \le N$ actual events occurring at times $t_1 \le t_2 \le .....t_n$, the partial likelihood that is to be maximized is given by :

$$L_{AG}(\underline{\beta}) = \prod_{i=1 \text{ to } n} \prod_{j=1 \text{ to } N} \{\{Y_j(t_i)\exp[\underline{x}_j(t_i)'\underline{\beta}]\} \div \sum_{u::Ri} \{Y_j(t_i)\exp[\underline{x}_j(t_i)'\underline{\beta}]\}$$

Where R_i is the risk set at time t_i^- (Andersen and Gill, 1982).

The Prentice, Williams and Peterson (PWP) Model

The Prentice, Williams, and Peterson (PWP) Model is an alternative to the Cox Proportional Hazards Model that has less stringent assumptions than the AG Model. Specifically, it allows both the baseline hazard and the values of the regression parameters to vary by event. This is accomplished through the use of stratification.

Strata are defined according to the number of previous events (Prentice, Williams, and Peterson, 1981).

As this thesis concerns the modelling of one recurrence of event, the number of previous events can be only 0 or 1. Let s = 0,1 index the number of preceding events, thus indicating the strata. The PWP Model formulates the intensity process, hence the change in the counting process over a small increment of time, separately for each stratum s:

$$\lambda_{sj}(t) = Y_{sj}(t)\, h_{s0}(t)\, \exp[\underline{x}_j(t)'\underline{\beta}_s]$$

Formulation of the PWP Model permits a separate such linking for each number of preceding events. Thus, the baseline hazard of an event varies depending on the number of preceding events. As well, the effect of the covariate pattern history can also vary with respect to the number of preceding events. Let s=0,1,......S index the number of preceding events. (Note: In this thesis, where interest is in the analysis of one recurrence of injury, s is either 0 or 1.)

The PWP Model further allows for time zero to be defined in various ways depending on the interest of the investigator. Prentice, Williams and Peterson suggest two definitions for time zero, the time t since the beginning of the study, and the time $t-t_{n(t)}$, the time since the immediately preceding event, which is often referred to as the gap-time model. Thus, the PWP Model formulates the instantaneous risk of an event at

time t as a function of the number of events history and the covariate pattern history as follows:

$$h(t, \beta, x(t) \mid n(t)=s) = h_{0s}(t)\exp(\underline{x}(t)'\underline{\beta}_s) \quad \text{and}$$
$$h(t, \beta, x(t) \mid n(t)=s) = h_{0s}(t-t_{n(t)-1})\exp(\underline{x}(t)'\underline{\beta}_s)$$

for the time since the beginning of the study and the time since the immediately preceding event respectively, where,

$s=0,1\ldots S$ = the number of preceding events
$h_{0s}(t)$ and $h_{0s}(t-t_{n(t)-1})$ = the corresponding baseline hazard functions for the two possible time scales
$\underline{\beta}_s$ = the vector of stratum specific regression coefficients.

The formulation of the PWP Model is most easily understood in the context of the derivation of the Cox Proportional Hazards Model. Recall first the Cox proportional Hazards Model link of the hazard function, h(•), to the explanatory variables $\underline{x}$ and the associated regression parameters $\underline{\beta}$:

$$h(t, \underline{\beta}, \underline{x}) = h_o(t) \exp[\underline{x}(t)'\underline{\beta}]$$

Recall next that the partial likelihood for the Cox Proportional Hazards Model is defined:

$$L_{partial} = \prod_{j=1 \text{ to } n} \{\exp[\underline{x}(t_{(j)})'\underline{\beta}] \div \textstyle\sum_{u: Rj} \exp[\underline{u}(t_{(j)})'\underline{\beta}] \}$$

The PWP Model adapts this partial likelihood, employing the stratification of number of previous events, where all individuals in a given strata are homogeneous with respect

to the number of preceding events. The corresponding partial likelihood equation for the time since the beginning of the study is therefore:

$$L_{PWP1} = \prod_{s=0 \text{ to } S} \prod_{k=1 \text{ to } ds} \{\exp[\underline{X}_{sk}(t_{sk})'\underline{\beta}_s] \div \sum_{u \in R(tsk,\, s)} \exp[\underline{X}_u(t_{sk})'\underline{\beta}_s] \} \quad \text{where,}$$

d_s = number of actual events occurring in the s^{th} stratum defined by the number of preceding events.

$R(t_{sk})$ = the subset at risk in the s^{th} stratum just prior to time t_{sk}.

For the gap-time choice of time scale, the PWP partial likelihood is expressed:

$$L_{PWP2} = \prod_{s=0 \text{ to } S} \prod_{k=1 \text{ to } ds} \{\exp[\underline{X}_{sk}(t_{sk})'\underline{\beta}_s] \div \sum_{u \in R(vsk,\, s)} \exp[\underline{X}_u(\mathscr{F}_u+v_{sk})'\underline{\beta}_s] \} \quad \text{where,}$$

$\mathscr{F}_u$ = the last failure time on subject u prior to entry into stratum s.

v_{sk} = the gap time from the immediately preceding event.

Maximum likelihood based inference for $\underline{\beta}_s$ are based on these partial likelihood equations.

CHAPTER 3

METHODS

Data Collection

The objective of this study was to collect retrospective data from a variety of sources on a dynamic population of Army Airborne soldiers in order to conduct a comprehensive morbidity evaluation. In order to accomplish this a relational database was designed and tested using EpiInfo prior to data collection. A parent file was constructed during October 1994 by obtaining an electronic roster of one brigade in the 82nd Airborne (n=2147) from the 82nd Airborne headquarters. A four digit unique identifier was created for each individual.

Abstraction of study data occurred during seven trips that occurred between November 1994 and March 1996. Different data sources were housed in different locations. Information in the Annual Health Questionnaires for Dental Treatment was located in the dental clinic: however, each battalion had its own medical clinic where individual medical records were located. Army Physical Fitness Test (APFT) score cards were housed in the company area, of which there were five per battalion.

Data were abstracted by making photocopies of each individuals' record from each data source. These photocopied records were then entered into EpiInfo and linked electronically to the parent file via the four digit unique identifier. Data sources were each individuals' outpatient medical records, Annual Health Questionnaire for Dental Treatment, and APFT score card. Additionally, demographic data were

extracted from the Total Army Injury and Health Outcomes Database (TAIHOD). Details on the data collection for each data source are given below.

Parent File

The parent file was constructed during October 1994 by obtaining an electronic roster of one brigade in the 82nd Airborne (n=2147). This brigade consisted of three, 671-person, battalions and a 134-person headquarters company. The original intent of this research was to conduct a comprehensive morbidity evaluation of the entire brigade: however logistical, budgetary and personnel constraints forced the medical record reviews to be conducted on only two battalions (n=1342). Therefore the available size of the parent file was limited to the individuals in these two battalions.

The dynamic nature of this population made it necessary to make some changes in the target population. Ninety-four (n=94) subjects were added to the parent file because information was found on these persons from at least one of the data sources. There were 162 subjects for whom data were unavailable from all data sources. These subjects were considered "non-arrivals" and were thus deleted from the parent file. This further reduced the functional size of the parent file (n=1274).

For the calculation of survival times, a roster of each individual's arrival date to the brigade was constructed by the Brigade Headquarters during March 1995. This enabled the calculation of each subject's time contribution to the study as the number of days between an individual's arrival date and January 31, 1995, the last day of the study

interval. Each individual's time contribution was limited by the length of the medical record review which was 396 days (13 months) for first battalion and 549 days (18 months) for second battalion. If an individual's arrival date occurred prior to the beginning date of the medical record review, their person time was truncated to the maximum allotted for their respective battalion. The arrival date to the brigade was available on all but 60 (4.7%) of the 1274 individuals on the parent file. Thus, the final analysis sample size for this thesis is n=1214.

Medical Records

The original intent of a February 1995 data collection trip was to conduct outpatient medical record reviews on the entire brigade for the 18 month interval, ending on January 31, 1995. However, logistical, budgetary and personnel constraints limited the review of the medical records to 2 of the 3 battalions. Additionally, the medical record review of one of these battalions was limited to 13 months.

Information specific to a medical problem was recorded on a pre-designed data collection form that included diagnosis; body part, if an injury, or physiological system, if an illness; number of follow-up visits; and highest level of medical provider seen for the problem.

Nine hundred-eighty (n=980, 80.7%) individuals' medical records were reviewed of the 1214 subjects in the functional parent file, during February 1995. An additional 185 (15.2%) of the medical records were reviewed during one of four data

collection trips that occurred between March and July of 1995, yielding a total of 1165 (96.0%) reviewed medical records.

Dental Records

Within each individual's dental record is a Health Questionnaire for Dental Treatment that is updated annually at the time of the individual's dental checkup. This questionnaire consists of 33 questions in which the individual can answer yes, no, or unknown. Two of these questions pertain to cigarette use and alcohol use and were the primary reason for abstracting these data.

One thousand five hundred ninety (n=1,590) dental questionnaires, representing approximately 74.0% of the brigade, were initially collected in November 1994. An additional 398 (18.5% of the brigade) dental questionnaires were found during one of four additional data collection trips between February and July of 1995, yielding a total of 1988 collected dental questionnaires. Of the 1214 subjects in the functional parent file, dental questionnaire data were collected on 1163 (95.8%).

Physical Fitness Data

The APFT score card is maintained for each individual at the company level. The APFT consists of a 2-minute timed push-up test, a 2-minute timed sit-up test and a 2-mile timed run. In addition to these data, information regarding the individual's height and weight are typically recorded on the APFT score card.

One thousand three hundred eighty three (n=1,383) APFT score cards, representing approximately 64.4% of the brigade, were initially collected in November 1994. An additional 262 APFT score cards (21.6% of the functional cohort) were found for individuals in either first or second battalions during one of three data collection trips between May 1995 and March 1996, yielding a total of 1645 collected APFT score cards. Of the 1214 subjects in the functional parent file, APFT score cards were collected on 1019 (83.9%).

The 1214 subjects in the functional parent file represent ten companies, each of which apparently had a different operating procedure regarding the recording of individuals' height and weight at the time of the APFT. Some recorded this information on the APFT score card, while some companies constructed separate rosters of these data. Of the 1214 subjects in the functional parent file, height and weight data were collected on 799 (65.8%).

Personnel Data

The Defense Manpower Data Center (DMDC) has been building a historical archive on all active duty soldiers since 1974. This database primarily contains demographic information on each individual. Much of these data were not available at either the brigade, battalion or company level on the population being studied and were thus extracted from this database. This personnel data is one of six databases that have been merged at the individual level to create TAIHOD (Amoroso, 1997). Of the 1214

subjects in the functional parent file, personnel files were successfully abstracted on 1202 (99.0%).

Data Entry

The medical review forms and the photocopied records from the dental questionnaires, jump logs and physical fitness score cards were entered into a pre-designed data entry system. After a computerized search for a subject within the parent file, a menu was utilized directing the data clerk to the appropriate data entry screen. The relevant data were entered and the data clerk returned to the parent file where a search could be conducted on the next individual. All data were entered in this manner two times, by two different individuals. After data entry was complete for a specific data source, the two entries of the data were compared electronically via either EpiInfo or SAS®. Discrepancies between the two data entries were corrected by checking the photocopy of the original data source.

Database Construction for Failure Time Analysis

The primary objective of this research was to investigate the risk factors for injury in the recurrent event setting. For this thesis interest is on injuries that occurred to either the lower extremity or low back and that were musculoskeletal (not poisoning or environmental) in nature, as these were the most common category of injury in the study population. As well, we were specifically interested in investigating if an injury

to a specific body part, increased the risk of a subsequent injury to either the same or adjacent body part. Five models were compared

1) Cox Proportional Hazards Model of the time of the first injury event.
2) Cox Proportional Hazards Model of the time of the first injury event to the time of the second injury event.
3) Prentice, Williams, and Peterson (PWP) Model of recurrent events in the two event setting.
4) Andersen-Gill Multiplicative Hazards (AG) Model of recurrent events in the two event setting.
5) Cox Proportional Hazards Model of the time of the last injury event.

Potential explanatory variables were extracted from the dental questionnaires, physical fitness score cards and personnel data sources. Self reported binary data regarding cigarette and alcohol use were taken from the dental questionnaire. The continuous variables corresponding to an individual's performance in the 2-minute timed push-up test, 2-minute timed sit-up test and 2-mile timed run were extracted from the physical fitness score card. Additionally, body mass index, a measure of body density, was calculated from each individual's anthropometric data.

Using the demographic information from the TAIHOD, age at entry to the study was calculated and was used as a covariate in the Cox Model for first injury event, the Cox model for final injury, the first stratum (first injury event) in the PWP model, and in the AG Model. Age at day of the first injury was also calculated, and was used as a covariate in the Cox Model for second injury and the second stratum (second injury event) in the PWP Model. A binary variable describing marital status and design variables, representing ethnicity were also constructed from the TAIHOD.

The referent group for ethnicity was Caucasian, and the design variables were representative of Blacks, Hispanics, and Other Ethnicity.

Selected potential explanatory variables were extracted from the medical records and were used in both the Cox Model for second injury and the second stratum (second injury event) in the PWP Model. These included type of first injury and highest level of medical provider seen. They were not used in the models specific to the first injury event because this information were measures of the sequelae of the first injury. We note that these variables could not be implemented in the AG Model because this model does not allow the list of covariates to differ by event.

A binary variable describing previous injury history during the study interval was created for the Cox Model for last injury.

Analysis

Preliminary analysis included the calculation of descriptive data for both the potential explanatory variables and the outcome of interest. Means and standard deviations were calculated for all continuous variables. Frequency and relative frequency distributions were computed for all discrete variables. The number of total traumatic, overuse, and unspecified pain injuries were calculated, as well as the number of specific injury diagnosis (i.e. fracture) in each of these groups. This information was also calculated separately for the first and second injury events. Chi-square tests were performed to test the differences in the proportion of injury type and specific diagnosis

between the first and second injury events. Similarly, the number of injuries to specific body parts were calculated, and chi-square tests were performed to test the differences in the proportion of affected body parts between the first and second injury events.

We hypothesized that the differing length of follow-up between the two battalions might necessitate that all regressions be stratified by battalion. Therefore, prior to model building, Kaplan-Meier estimates of the survivor function, as well as log-rank tests were computed to determine if there were significant differences in these distributions by battalion.

The approach used for model building was similar for all three models. A stepwise procedure was implemented so that the number of independent variables would be reduced to only those that may be statistically significant. The stepwise procedure implemented a p-value for entry at 0.25 and a p-value for removal at 0.80. The high p-value for removal was used so that potential confounders would not be prematurely removed from the analysis. If a design variable remained in the model after the execution of the stepwise procedure, all design variables associated with the original categorical variable were retained. Starting with the remaining independent variable with the largest Wald Chi-square p-value, variables were individually removed from the model. The log-likelihood test was implemented to determine model improvement. If the removal of a variable created a change of greater than 20% to the coefficient of another covariate, that variable was considered to be a confounder and

was retained in the model. Design variables associated with a single categorical variable that were non-significant and non-confounding were removed from the model as a group. After ascertainment of the best main effects model, the scale of continuous variables was assessed using smoothed scatter plots of the Martingale residual for the model against the continuous variable of interest. Clinically plausible interactions were explored and added to the model if statistically significant.

After the best model was determined for each analysis of interest, the proportional hazards assumption was tested for each predictor in each model. The proportional hazards assumption was tested by adding a variable representing the interaction of the predictor with the logarithm of the time. Significance levels less than 0.05 suggested tentatively a violation of the proportional hazards assumption. For predictors violating the proportional hazards assumption according to this test, a log-cumulative hazard plot, a plot of the negative logarithm of the estimated survivor function against the logarithm of the survival time, was constructed (Collett, 1994). In order to construct these plots for continuous variables, the variable was divided into quartiles. Near parallel curves suggested that the violation of proportionality was not severe and could be reasonably ignored.

In developing a Cox Model of the time to last injury, we sought to determine if previous injury history within the study interval was a risk factor for subsequent history. Initially, a crude hazard ratio was calculated by having only the variable representing previous injury history as a dependant variable. This hazard ratio was then

adjusted with respect to explanatory variables that were significant in either the Cox Model to first event, the Cox Model to second event, the PWP Model, or the AG Model. The rational for this alternative approach to model development was to calculate the increased risk for injury that was attributable to having a recent (within the study interval), previous injury. Additionally the effect of previous injury history on predictors from the other models could be examined.

CHAPTER 4

RESULTS

Demographics

Descriptive characteristics of the study population are presented in Table 1. This is an all-male, predominately white, physically fit, young population. The average age at entry to the study interval was approximately 24.0 (SD=5.0) years. The average performance for the 2-minute timed push-up test and the 2-minute timed sit-up test were 66.8 (SD=12.8) and 69.6 (SD=11.3) repetitions, respectively. The mean performance for the 2-mile timed run was 13.7 (SD=1.3) minutes. The average height, weight and body mass index, a measure of body density, were 1.76 (SD=0.07) meters, 76.11 (SD=9.52) kilograms and 24.48 (SD=2.57) kg/meters^2. More than half of the population reported that they were alcohol users and 30% reported that they were cigarette smokers. Approximately 38% were married and 79% were Caucasian.

TABLE 1 - Descriptive Data

	n	mean	SD
Age at entry to study interval (years)	1202	23.97	5.00
Push-ups (repetitions in 2 minutes)	1014	66.83	12.80
Sit-ups (repetitions in 2 minutes)	1018	69.58	11.32
Run time (minutes for 2 miles)	1011	13.69	1.32
Height (meters)	799	1.76	0.07
Weight (kilograms)	799	76.11	9.52
Body Mass Index (KG/meters^2)	799	24.48	2.57

continued next page

TABLE 1 (Continued)

	n	% yes
Male gender	1214	100%
Current alcohol user	1159	55.2%
Current cigarette user	1160	30.4%
Married	1201	38.0%
Ethnicity - White Black Hispanic Other	946 125 64 67	78.7% 10.4% 5.3% 5.5%

Injury

There were a total of 919 injuries during the study interval, 809 (88.0%) of which were musculoskeletal injuries; the remaining 110 (12.0%) were either environmental injuries or could not be classified in either group. Five hundred seventy five (n=575) of the 919 total injuries occurred to either the lower extremities or the low back, 520 (90.4%) of which were musculoskeletal in nature. Column I in Table 2 summarizes the number of uncensored observations available for modeling each injury event; while column II shows the distribution of the multiple events. Only the 460 musculoskeletal injuries to the lower extremity or low back occurring as either a first or second event, constituting 88.5% of the 520 lower extremity or low back, musculoskeletal injuries were of interest in this thesis. These injury events are denoted in bold face type in Table 2.

TABLE 2 - Injury Events Available for Analyses (I) and Distribution of Multiple Injuries (II)

Number of Injury Event	I Number of Study Subjects Experiencing this Event	II Number of Study Subjects for whom this is Event Total
0	**875**	**875**
1	**339**	**218**
2	**121**	**74**
3	47	35
4	12	11
5	1	1

Table 3 summarizes the periods of follow-up. The mean time contribution for members of first battalion was 340.8 days (SD=96.4) and ranged from 21 to 396 days. Members of second battalion contributed an average of 397.3 days (SD=165.6) ranged from 19 to 549 days. Table 3 also summarizes the distribution of injury event numbers by battalion. For the analysis of the first injury, there were 339 events and 875 censored individuals. There were 121 events and 218 censored subjects for the analysis of the second event. The distribution of the number of injury events did not differ by battalion.

Table 4 summarizes specific injury diagnosis by category (traumatic, overuse or unspecified pain) for all lower extremity and low back, injuries. First and second injury events are separately displayed. The percentage of total injuries, as well as the percentage by injury category, is given for each diagnosis. Chi-square tests suggest that the proportion of first and second injury events are not statistically different in terms of either injury categories or specific diagnosis.

TABLE 3 - Contribution of the Analysis of Time to Event by Battalion

	1st Battalion	2nd Battalion	Total
Person Time (days)			
n	614	600	1214
mean	340.8	397.3	368.7
SD	96.4	165.6	138.0
min	21	19	19
max	396	549	549
Analysis of 1st Injury			
# of Events	170	169	339
# Censored	444	431	875
Total	614	600	1214
Analysis of 2nd Injury			
# of Events	60	61	121
# Censored	110	108	218
Total	170	169	339

Information regarding the frequency of injuries to specific joints or muscle groups is in Table 5. The most common body parts injured were the ankle, knee, low back, and foot (including the toes), and together accounted for 402 (87.4%) of the 460 injuries of interest. The proportions of all injuries that occurred to the lower leg (shin and calf) were not homogeneous between the first and second injury events (Chi-squarep=.026), with 24 of the 26 injuries (92.3%) occurring to this region as the first

injury. There were no significant difference in the proportions of injuries between first and second injury events for all other body parts.

TABLE 4 - Injury Type and Diagnosis for Total Lower Extremity/ Low Back Musculoskeletal Injuries and by Event (Injury) Number

Injury Category	Diagnosis	Total n (% of total inj) (% of inj type)	1st Event n (% of total inj) (% of inj type)	2nd Event n (% of total inj) (% of inj type)
Traumatic	Sprain/Strain	203 (44.1) (70.7)	151 (44.5) (71.9)	52 (43.0) (68.4)
	Contusion	35 (7.6) (12.2)	23 (6.8) (11.0)	11 (9.1) (14.5)
	Fracture	20 (4.3) (7.0)	13 (3.8) (6.2)	7 (5.8) (9.2)
	Abrasion/Laceration	10 (2.2) (3.5)	9 (2.7) (4.3)	1 (0.8) (1.3)
	Other	19 (4.1) (6.6)	14 (4.1) (6.7)	5 (4.1) (6.6)
	TOTAL	*287 (62.4)*	*210 (61.9)*	*76 (62.8)*
Overuse	Unspecified	41 (8.9) (37.7)	28 (8.3) (35.9)	13 (10.7) (41.9)
	Strain	31 (6.7) (28.4)	25 (7.4) (32.0)	6 (5.0) (19.4)
	Stress Fx/Rxn	14 (3.0) (12.8)	11 (3.2) (14.1)	3 (2.5) (9.7)
	Tendinitis	11 (2.4) (10.1)	6 (1.8) (7.7)	5 (4.1) (16.1)
	Other	12 (2.6) (11.0)	8 (2.4) (10.3)	4 (3.3) (12.9)
	TOTAL	*109 (23.0)*	*78 (23.0)*	*31 (25.6)*
Pain	Unspecified	64 (13.9)	51 (15.0)	13 (10.7)
Totals		**460**	**339**	**121**

TABLE 5 - Body Part Affected for Total Lower Extremity/ Low Back Musculoskeletal Injuries and by Event (Injury) Number

Body Part Affected	Total n (% of total inj)	1st Event n (% of total inj)	2nd Event n (% of total inj)
Ankle	112 (24.3)	88 (26.0)	24 (19.8)
Knee	105 (22.8)	72 (21.2)	33 (27.3)
Low Back	95 (20.7)	71 (20.9)	24 (19.8)
Foot / Heel / Toe	90 (19.6)	61 (18.0)	29 (24.0)
* Shin / Calf	26 (5.7)	24 (7.0)	2 (1.7)
Hip	17 (3.7)	10 (2.9)	7 (5.8)
Thigh	11 (2.4)	9 (2.7)	2 (1.7)
Multiple Low	4 (0.9)	4 (1.2)	0 (0.0)
Totals	**460**	**339**	**121**

* denotes a significant difference ($p<.05$) of the proportion of affected body parts by event

Failure Time Regression Analyses

Figure 2 shows the Kaplan-Meier estimates of time to first injury for the two battalions and suggests that they are similar. Kaplan-Meier estimates of the survivor function stratified by battalion for the other models yielded similar findings (data not shown). Log-rank tests for equality of survivor functions confirmed that there is not a significant difference between the two battalions for any model. Chi-square p-values ranged from 0.37 to 0.83 for the five failure time models.

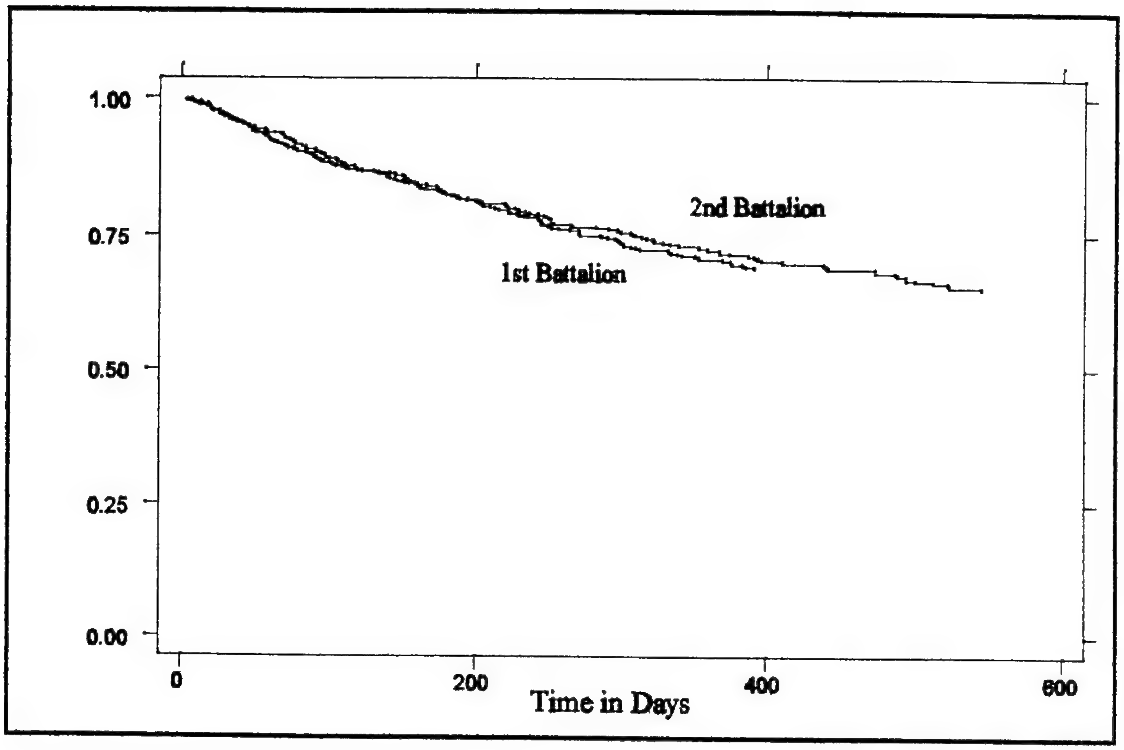

Figure 2 - Kaplan-Meier Survivor Estimates of Time to First Injury Event, by Battalion

Cox Model to First Event

The Cox Model of the time to first injury resulted in a model that suggests that increased hazard of injury is associated with lower push-up performance, lower sit-up performance, and younger age at entry to study. Also predictive of increased hazard were use of alcohol and being married (Table 6). Specifically, a ten unit decrease in upper body strength and endurance as measured by the 2-minute timed push-up test resulted in a 16.2% increased risk of lower extremity musculoskeletal injury ($P < .01$). Similarly, a ten unit decrease in abdominal and hip flexor strength and endurance as measured by the 2-minute timed sit-up test resulted in a 15.2% increased risk of injury

(P < .05). A 1-year increase in age resulted in a 4.1% decrease in risk of lower extremity injury (P < .01). Alcohol non-abstainers were at 30.4% greater risk of injury (P < .05). There is evidence that married subjects had a relative odds of injury 27.0% greater than that of their unmarried counterparts (P < .10). This variable was retained in the final model primarily because of its marginal significance and that it was a confounder on the variable, age at entry to study. Removal of the marital status variable from the model resulted in a 32.0% change in the parameter estimate for age (data not shown).

TABLE 6 - Parameter Estimates for Final Cox Regression Model: First Injury

	Parameter Estimate	SE	Hazard Ratio (95% CI)
Push-ups (10 repetition decrease)	0.150 ***	0.056	1.162 (1.042, 1.296)
Sit-ups (10 repetition decrease)	0.142 **	0.063	1.152 (1.018, 1.305)
Age at entry to study (1 year increase)	-0.040 ***	0.015	0.961 (0.933, 0.989)
Alcohol user (vs. abstainer)	0.265 **	0.121	1.304 (1.028, 1.653)
Married (vs. non-married)	0.239 $*	0.141	1.270 (0.963, 1.675)

Model Chi-Square = 37.660, 5df (p=0.0001)
*P< .1 **P< .05 ***P< .01 $confounded with age

Cox Model to Second Event

The Cox Model, from the time of the first injury to either the time of the second injury or to the end of study interval, if there was no additional injury, suggested that the following were associated with a repeat injury: decreased push-up performance, traumatic first injury, and Medic as the highest level of provider for the first injury.

Hispanics were at increased risk and individuals in the "Other" ethnicity category were at lower risk (Table 7). A ten unit decrease in upper body strength and endurance as measured by the 2-minute timed push-up test resulted in a 24.9% increased risk of subsequent injury ($P < .01$). If the subject's first injury was categorized as a traumatic injury, there was an 83.4% increased risk of subsequent injury than if the first injury was categorized as overuse or unspecified pain ($P < .01$). Subjects who saw only a Medic, the lowest level of medical provider, for the preceding injury were 71.6% more likely to undergo a subsequent injury ($P < .05$). Hispanic individuals had greater than four times the risk of experiencing a second lower extremity injury than did Caucasian individuals ($P < .001$). Two thirds of the Hispanic subjects who were at risk to experience a second lower extremity injury did so, compared to 34.3% of the remainder of the subjects (data not shown).

TABLE 7 - Parameter Estimates for Final Cox Regression Model: Second Injury

	Parameter Estimate	SE	Hazard Ratio (95% CI)
Push-ups (10 repetition decrease)	0.223 ***	0.083	1.249 (1.062, 1.470)
Previous Traumatic Injury	0.607 ***	0.217	1.834 (1.200, 2.804)
Highest level of Medical Provider from Previous Injury: Medic (vs all others)	0.540 **	0.251	1.716 (1.049, 2.808)
Ethnicity (referent = White): Black	0.037	0.374	
Hispanic	1.446 ****	0.368	4.246 (2.023, 8.738)
Other	-1.243 *	0.726	0.289 (0.070, 1.120)

Model Chi-Square = 31.629, 6df (p=0.0001)
*P< .1 **P< .05 ***P< .01 ****P< .001

Andersen-Gill (AG) Model

Associated with increased hazard of injury in the AG Model were decreased push-up performance, decreased sit-up performance, younger age at entry to study, current use of alcohol, and being married. Table 8 shows that a ten unit decrease in the 2-minute timed push-up test resulted in a 18.1% increased risk of lower extremity musculoskeletal injury (P < .001). Similarly, a ten unit decrease in the 2-minute timed sit-up test resulted in a 11.5% increased risk of injury (P < .05). A 1-year increase in age resulted in a 3.7% decrease in risk of injury (P < .01). Married subjects were at 27.1% greater risk of injury (P < .05). There is evidence that alcohol users were marginally more likely (18.6%) to be injured than the subjects that were alcohol abstainers (P < .10); however this variable was retained in the final model because it was a confounder on the effect of sit-up performance. Removal of the alcohol use variable from the model resulted in a 24.0% change in the parameter estimate for sit-up performance.

TABLE 8 - Parameter Estimates for Final Andersen-Gill Model

	Parameter Estimate	SE	Hazard Ratio (95% CI)
Push-ups (10 repetition decrease)	0.167 ****	0.048	1.181 (1.076, 1.296)
Sit-ups (10 repetition decrease)	0.109 **	0.054	1.115 (1.003, 1.241)
Age at entry to study (1 year increase)	-0.036 ***	0.013	0.964 (0.941, 0.988)
Married (vs. non-married)	0.240 **	0.120	1.271 (1.005, 1.608)
Alcohol user (vs. abstainer)	0.171 $*	0.104	1.186 (0.968, 1.455)

Model Chi-Square = 43.798, 5df (p=0.0001)
*P< .1 **P< .05 ***P< .01 ****P< .001 $confounded with sit-ups

Prentice Williams and Peterson (PWP) Model

The PWP resulted in a model that was identical to the combination of the Cox Model of the first event and the Cox Model of the second event (Table 9). The first stratum included persons with a history of zero events; the second stratum included only those persons with a first injury.

TABLE 9 - Parameter Estimates for Final PWP Model

Stratum=1 (1st Injury)	Parameter Estimate	SE	Hazard Ratio (95% CI)
Push-ups (10 repetition decrease)	0.150 ***	0.056	1.162 (1.042, 1.296)
Sit-ups (10 repetition decrease)	0.142 **	0.063	1.152 (1.018, 1.305)
Age at entry to study (1 year increase)	-0.040 ***	0.015	0.961 (0.933, 0.989)
Alcohol user (vs. abstainer)	0.265 **	0.121	1.304 (1.028, 1.653)
Married (vs. non-married)	0.239 $*	0.141	1.270 (0.963, 1.675)
Stratum=2 (2nd Injury)			
Push-ups (10 repetition decrease)	0.223 ***	0.083	1.249 (1.062, 1.470)
Previous Traumatic Injury	0.607 ***	0.217	1.834 (1.200, 2.804)
Highest level of Medical Provider from Previous Injury: Medic (vs all others)	0.540 **	0.251	1.716 (1.049, 2.808)
Ethnicity (referent = White): Black	0.037	0.374	
Hispanic	1.446 ****	0.368	4.246 (2.023, 8.738)
Other	-1.243 *	0.726	0.289 (0.070, 1.120)

Model Chi-Square = 69.289, 11df (p=0.0001)
*P< .1 **P< .05 ***P< .01 ****P< .001 $confounded with age (1st stratum)

Cox Model of Time to Last Injury

The purpose of the Cox Model of time to last injury was to determine the magnitude of the increased hazard associated with previous injury history. Table 10

shows both crude and adjusted values of parameter estimates, standard errors and hazard ratios for the history of previous injury, as well as for significant variables in any of the multiple event modelling strategies previously conducted. The adjusted value is adjusted for variables that were statistically significant in any one of these models, which included push-up performance, sit-up performance, age at entry to study, alcohol user (vs. abstainer), marital status and ethnicity. The variables describing previous traumatic injury, and highest level of provider for the previous injury that were included in the Cox Model for second injury and the second stratum (second injury event) in the PWP Model were not included in this model. This is because the last injury event is not the second injury event for all individuals. The crude and adjusted parameter estimate values corresponding to previous injury history did not differ considerably, suggesting that its effect is independent of those of the other predictors of recurrent injury and that individuals with a history of one injury are at approximately seven times greater risk of a second injury.

The effect of previous injury history is perhaps easier to interpret by examination of a log-rank test for equality of the survivor functions between those with a prior injury history versus those without a prior injury history. Table 11 illustrates that if previous injury history was not a risk factor for subsequent injury, only 25 of the 339 injury events would have been a second injury event. The actual number of second injury events (individuals with a previous injury history) was 121, a value that is almost five times greater than the expected number of subjects with previous injury history.

TABLE 10 - Crude and Adjusted Parameter Estimates for History of Previous Injury and Other Covariates from Cox Regression Model for Last Injury

		Parameter Estimate	SE	Hazard Ratio (95% CI)
History of Previous Injury	**(crude)**	**2.005*******	**0.117**	**7.426 (5.905, 9.338)**
	(adjusted)	**1.941*******	**0.130**	**6.965 (5.394, 8.992)**
Push-ups (10 rep decrease)	(crude)	0.204****	0.046	1.227 (1.121, 1.342)
	(adjusted)	0.058	0.055	1.060 (0.951, 1.181)
Sit-ups (10 rep decrease)	(crude)	0.207****	0.052	1.230 (1.110, 1.363)
	(adjusted)	0.156**	0.065	1.169 (1.030, 1.327)
Age (1 yr increase)	(crude)	-0.033***	0.012	0.968 (0.945, 0.990)
	(adjusted)	-0.038**	0.015	0.963 (0.935, 0.991)
Alcohol user (vs. abstainer)	(crude)	0.107	0.111	1.113 (0.895, 1.385)
	(adjusted)	0.290**	0.123	1.337 (1.051, 1.701)
Married (vs. non-married)	(crude)	-0.022	0.112	0.978 (0.785, 1.218)
	(adjusted)	0.080	0.139	1.083 (0.824, 1.423)
Ethnicity : Black:	(crude)	-0.093	0.185	0.911 (0.635, 1.308)
	(adjusted)	0.244	0.221	1.277 (0.828, 1.968)
Hispanic:	(crude)	-0.164	0.265	0.849 (0.505, 1.428)
	(adjusted)	-0.125	0.298	0.883 (0.492, 1.582)
Other:	(crude)	-0.122	0.258	0.885 (0.534, 1.466)
	(adjusted)	0.209	0.289	1.232 (0.700, 2.170)

Model Chi-Square for history of previous injury (crude) = 228.15, 1df (p=0.0001)
Model Chi-Square for history of previous injury (adjusted) = 220.44, 9df (p=0.0001)
$^{*}P< .1$ $^{**}P< .05$ $^{***}P< .01$ $^{****}P< .001$ $^{*****}P< .0001$

TABLE 11 - Log-Rank Test for Equality of Survivor Functions for Previous Injury History

	Observed	Expected
No previous injury history	218	314
Previous injury history	121	25
Totals	339	339

Chi-square = 400.5, 1df (p < 0.0001)

Proportional Hazards Assumption

An underlying assumption of the Cox Model is that the survival time among individuals in two or more different groups of a significant variable are proportional to one another. Since the multiple event models reduce to the Cox Model in the absence of more than one event, it is reasonable to examine this assumption for all of the above statistical models that were used to examine injury risk factors in a setting where individuals may have sustained more than one injury. One method of testing this assumption is by adding a covariate to the final model that is representative of the interaction between the covariate of interest and the logarithm of the time variable. If this interaction term has a corresponding small P-value (< .05), one would conclude that the survival time between individuals with different values of this covariate are not proportional. In other words, the effect of this covariate is not the same at all points in time.

Variations of the effect of a covariate with time may, however, not be of concern. The parameter estimates for a significant covariate represents the average effect of that covariate over the range of time observed in the data (Allison et al., 1995). Apparent violations of the proportional hazards assumption were therefore checked via log-cumulative hazard plots for each of the above models. This is a plot of the negative logarithm of the estimated survivor function on the vertical axis against the logarithm of the time variable on the horizontal axis (Collett, 1994). Figures 3, 4, 5, and 6 are the log-cumulative hazard plots for all significant variables in the Cox Model

to first injury, the Cox Model to second injury, the AG model, and the Cox Model to each individuals last injury, respectively. Variables representing quartiles were used to construct plots for continuous variables. These plots for the PWP Model are identical to the Cox Models to the two separate injury events (Figures 3 and 4) and are, therefore, not shown separately. Only plots representing the significant covariates in the adjusted model are shown for the Cox Model to an individual's last injury (Figure 6).

Notice that the different strata in each log-cumulative hazard plot do not vary greatly from one another. The small divergences between the different curves on each plot represent that the survival times between individuals in these different groups may not be perfectly proportional; however this also exhibits that this non-proportionality is not of concern in this setting.

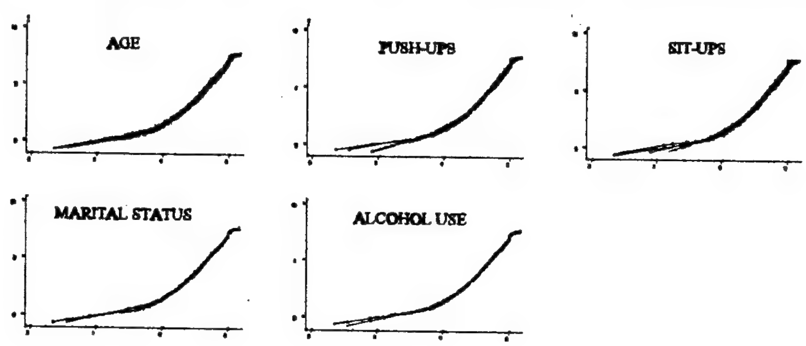

Figure 3 - Log-Cumulative Hazard Plots for Cox Model to First Injury

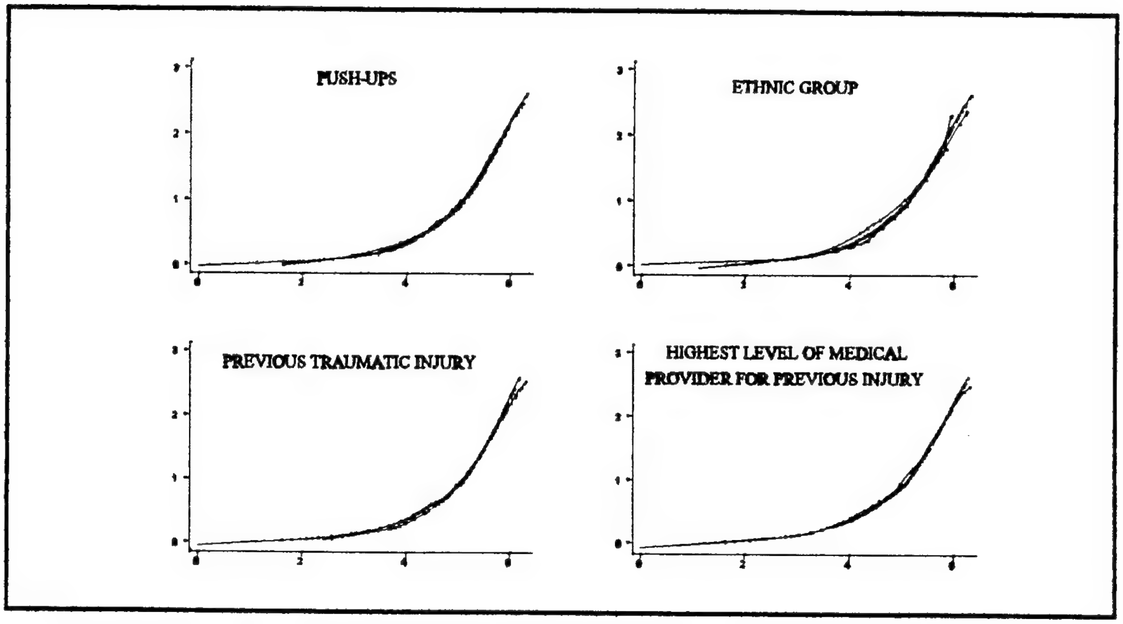

Figure 4 - Log-Cumulative Hazard Plots for Cox Model to Second Injury

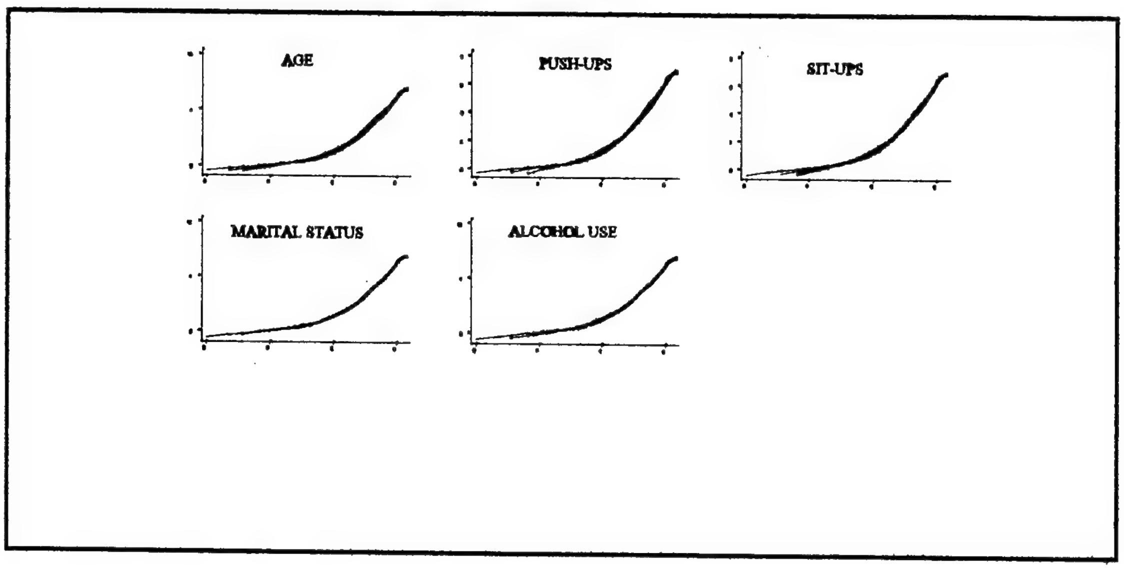

Figure 5 - Log-Cumulative Hazard Plots for Andersen-Gill Model

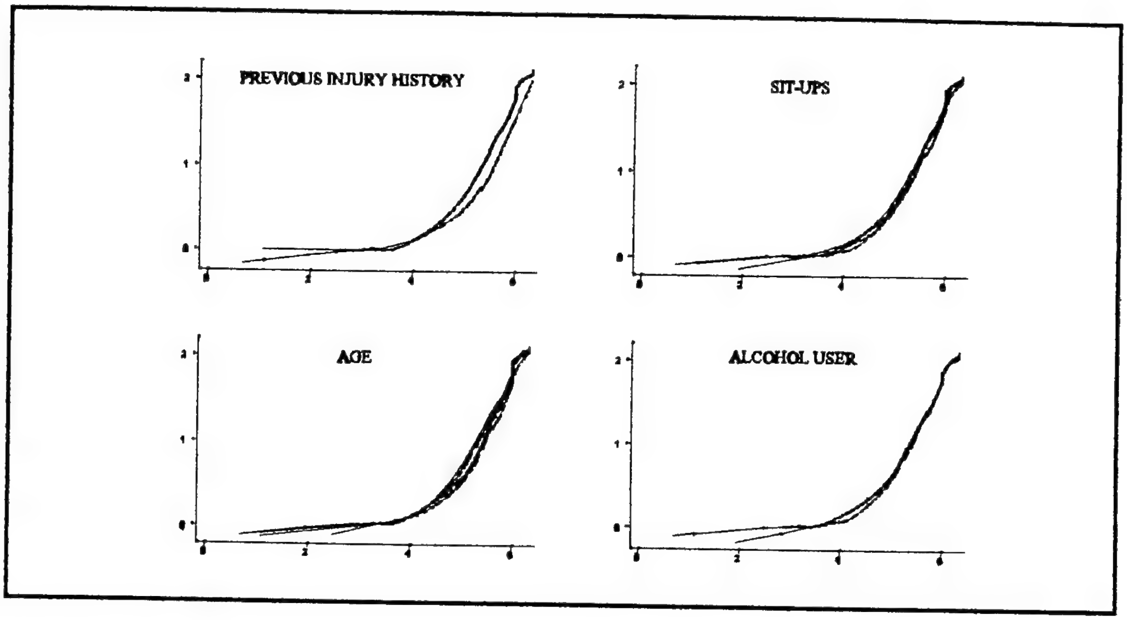

Figure 6 - Log-Cumulative Hazard Plots for Cox Model to Last Injury

CHAPTER 5

DISCUSSION

Comparison of Results

When comparing the results from the different models used for the multiple injury event analysis, the most noteworthy observation is that the PWP Model is equivalent to the combination of the two Cox Models used for the two separate injury events. Specifically, parameter estimates for the first stratum of the PWP Model are equal to those of the Cox Model of the first event (Table 12). The same is true for the second stratum of the PWP Model when compared to the Cox Model of the time between the first and second events. Additionally, the model chi-square statistic for the PWP Model is exactly the sum of the model chi-square statistics from the two separate Cox Models.

TABLE 12 - Comparison of Parameter Estimates Between Three Models

	Cox (first Injury) Parameter est. (SE)	PWP (first strata) Parameter est. (SE)	AG Parameter est. (SE)
Push-ups (10 repetition decrease)	0.150 (0.056) ***	0.150 (0.056) ***	0.167 (0.048) ****
Sit-ups (10 repetition decrease)	0.142 (0.063) **	0.142 (0.063) **	0.109 (0.054) **
Age at entry to study (1 year increase)	-0.040 (0.015) ***	-0.040 (0.015) ***	-0.036 (0.013) ***
Alcohol user (vs. abstainer)	0.265 (0.121) **	0.265 (0.121) **	0.171 (0.104) &*
Married (vs. non-married)	0.239 (0.141) $*	0.239 (0.141) $*	0.240 (0.120) **

*P< .1 **P< 05 ***P< .01 ****P< .001

$confounded with age &confounded with sit-ups

Having determined that the PWP Model is equivalent to the combination of the two Cox Models, the AG model can now be compared to either of these. For simplicity it will be compared to only the PWP Model. In this data set, development of an AG Model yielded the same set as predictors as obtained from the first stratum of the PWP model. This is consistent with a study that implemented the AG Model to determine if exercise reduced the occurrence of falls experienced by elderly individuals. In this study the AG Model was compared to a Cox Model of time to first fall to ensure that multiple fallers did not unduly influence the results (Province et al., 1995). Table 12 displays the parameter estimates for these models. Recall that push-up performance was the only independent variable that remained in both strata of the PWP Model. The influence of this covariate on injury, regardless of the event number, is evident by both the increased parameter estimate and increased significance of the corresponding p-value as compared to those from a model that looks at only the first injury event. The rest of the parameter estimates in the AG Model, with the exception of marital status, are closer to zero than the parameter estimates in the first stratum of the PWP Model. Recall that none of these variables were significant risk factors for the second injury event. Thus in this data set, the parameter estimates from the AG Model are primarily influenced by the first event. This is likely true because of the substantial decline in the number of subjects having a second injury as compared to those with a first injury. In a setting where virtually all individuals had multiple events or where risk factors are

equivalent from one event to the next, the AG Model would perhaps be more useful, provided the assumption of the common baseline hazard is reasonable.

Benefits of the PWP Model

The PWP Model is the most useful of the three methods employed to analyze these data and perhaps, more generally, data in the multiple injury event setting. This model has the benefit of permitting a different baseline hazard function for each event. Table 13 displays the parameter estimates for the final PWP Model, as well as for a "comparison" model that includes, in both strata, all covariates that were significant in either stratum. In this manner, changes in the parameter estimates from one injury to the next can be easily compared. Table 13 also shows the percentage of change in the parameter estimates between the final and comparison model where applicable. There was no significant confounding of parameter estimates between the two models.

A practical advantage of the PWP model is inherent within the structure of the database. Specifically, Kaplan-Meier survivor estimates to the time of injury can easily be plotted on the same axis. Figure 7 shows that the estimated survivor function for the first injury is consistently less than that of the second injury. This suggests that once an individual experiences a traumatic injury to the lower extremity or low back, he is at greater risk to undergo a similar subsequent injury. The results of the log-rank for the equality of the survivor function between the two strata in the PWP Model are shown in Table 14. This specifies that of the 460 injuries of interest, 55 of them are

expected to be an individual's second injury, however the actual number of second injuries is 121, more than twice the expected number. This yields information that is similar to that from log-rank test conducted on the binary variable previous injury in conjunction with the Cox Model to last injury (refer to Table 11).

TABLE 13 - Parameter Estimates for Final and "Comparison" PWP Models

	Parameter Estimate for Final Model	Parameter Estimate for "Comparison Model"	% Change in Parameter Estimate
Push-up stratum=1 Push-up stratum=2	0.150*** 0.223***	0.148*** 0.270***	-1.35 % 17.41 %
Sit-up stratum=1 Sit-up stratum=2	0.142** NA	0.143** 0.068ns	0.70 % NA
Age stratum=1 Age stratum=2	-0.040*** NA	-0.039*** -0.023ns	-2.56 % NA
Alcohol stratum=1 Alcohol stratum=2	0.265** NA	0.260** -0.203ns	-1.92 % NA
Marital Status stratum=1 Marital Status stratum=2	0.239$* NA	0.241* 0.173ns	0.83 % NA
Ethnicity (referent=white) Black stratum=1 Black stratum=2 Hispanic stratum=1 Hispanic stratum=2 Other stratum=1 Other stratum=2	 NA 0.037ns NA 1.446**** NA -1.243*	 -0.018ns 0.034ns -0.246ns 1.530**** -0.132ns -1.240*	 NA -8.82 % NA 5.49 % NA -0.24 %
Prev traum injury stratum=1 Prev traum injury stratum=2	NA 0.607***	NA 0.584***	NA -3.94 %
Prev Provdr- medic stratum=1 Prev Provdr- medic stratum=1	NA 0.540**	NA 0.612**	NA 11.76 %

*P< .1   **P< 05   ***P< .01   ****P< .001   ns P > .1
NA = Not Applicable $confounded with age

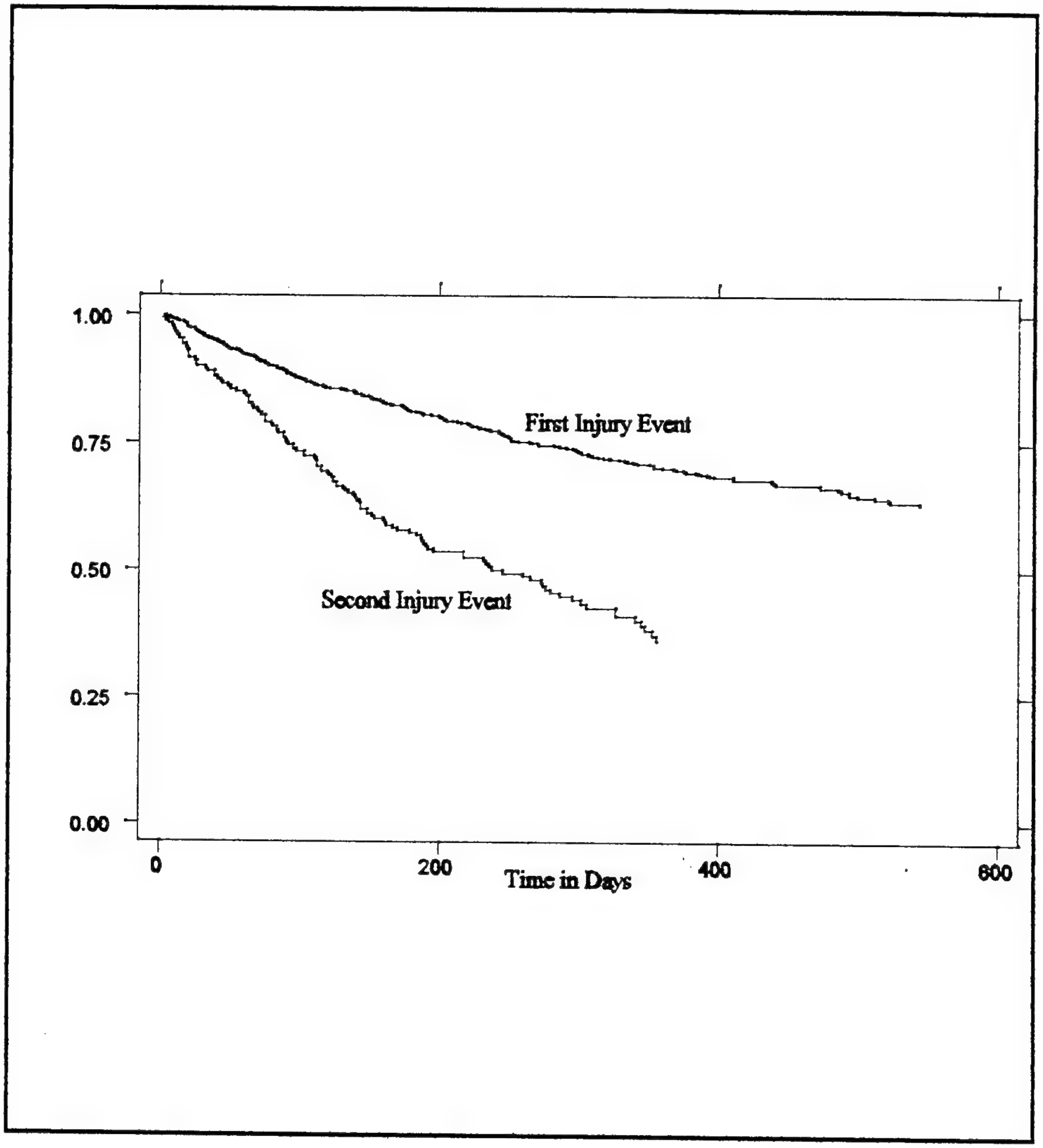

Figure 7 - Kaplan-Meier Survivor Estimates for the Two Strata (Injury Events) in the PWP Model

TABLE 14 - Log-Rank Test for Equality of Survivor Functions between the Two Strata (Injury Events) in the PWP Model

	Observed	Expected
Stratum 1 (first injury)	339	405
Stratum 2 (second injury)	121	55
Totals	460	460

Chi-square = 89.49, 1df ($p < 0.0001$)

Benefits of the Cox Model of the Time to Last Injury

While the PWP model is the best for analyzing recurrent injuries, it does have one limitation. Specifically, the increase in hazard attributable to having a previous injury is not directly estimable. The PWP model does allow for verification that there is an increased risk for injury having had a previous injury by way of Kaplan-Meier estimates of the survivor function and log-rank tests of the different strata (injury events). However, the Cox Model of the time to the last injury event is needed to fully understand the effect of previous injury history on subsequent injury, as it is the only model that was examined in this thesis in which the increase hazard associated with having had a previous injury can be estimated.

Comparison of the Multiple Event Models: Summary

Table 15 compares many aspects of the three methods of multiple event failure time analysis employed in this thesis. The prominent component in the comparisons of the three methods is that the underlying process of the PWP Model is the same as using two Cox Models, where to be included in the second model, a subject must have

experienced a prior event. The PWP Model accomplishes this by stratifying the model by the event number. In both of these approaches, the baseline hazard differs by event. The AG Model is different from the other models in its assumptions of a common baseline hazard and covariate effects across strata.

Each of these models has some unique qualities with respect to the construction of the respective databases required. The Cox Model is the simplest; the primary need is a well defined dichotomous censoring variable, which in this thesis, was the absence or presence of a traumatic lower extremity or low back injury. In order to be in the following model, an individual must have had an event of interest in the preceding model. The database needed for the PWP model is easy to construct by concatenating the two separate Cox Models. Prior to joining these, a variable specifying the event number must be added to the respective databases; this becomes the stratification variable. Additionally, all variables that occur in more than one stratum must be renamed so that there are no explanatory variables that have coinciding names between strata. After the databases are appended, assure that all variables that do not correspond with the strata do not have missing data. In other words, a variable that is specific to the first stratum must have a value in the second stratum. This prevents the subject from being unnecessarily discarded in the analysis. It is simple to place a common value, such as "0" for all variables that are in this state. The AG Model is complicated due to the database management involved with the counting process. Each event is considered independent; therefore, in the presence of multiple events, the

time contribution of an event other than the first begins at the time of the immediately preceding event. Samples of the databases used for these analysis can be found in Appendix 1. Included in these samples are the following variables: ID, Status (the censoring variable), Time (Time start and Time stop for the Andersen-Gill data), and the independent variables Age and Alcohol drinker. Age for the Cox Model to second injury event and for the second strata of the PWP Model is the age at the time of the preceding injury, not the age at entry to the study.

There are no obstacles in the construction of the best statistical model in any of the methods discussed. In all cases, model building can proceed in the same manner as in other types regression analysis. Statistical software enables model building to be performed manually, or stepwise, and best subsets options are also available for all three models. For the PWP Model, regardless of the method of model building chosen, failure to stratify by event number will produce erroneous results.

The interpretation of the final models, as well as the inferences drawn, appear to be logical for the two separate Cox Models as well as the PWP Model. This is because of the separate baseline hazard and parameter estimate for each event. The AG Model is limited by the facts that all events share the same baseline hazard, the list of covariates cannot vary by event, and that only one parameter estimate is produced. Additionally, this parameter estimate is strongly influenced by the first event in a multiple injury setting. Specifically, in a multiple injury setting where the number of first events is disproportonally larger than the number of second events,

TABLE 15 - Comparisons of theThree Methods of Time Dependent Multiple Event Analysis

	2 Separate Cox Models	PWP	AG
Underlying Process	•To be in 2nd model must have had a prior injury •Different baseline hazards for each event	•To be in 2nd model must have had a prior injury •Different baseline hazards for each event	•Counting Process •Independent event times •Baseline Hazard does not vary by event
Database Construction	Easiest: 2 separate models	Increased difficulty: rename variables common to both events, add a strata variable, combine the data from the 2 separate events, and set the value of variables that do not belong to the corresponding strata to "0"	Increased difficulty: complicated due to counting process, time "stop" foe event #1 equals time "start" for event #2.......etc.
Model Building	Straight forward	Must remember to stratify by event number	Straight forward
Interpretation	Separate hazard ratios for each event	Separate hazard ratios for each strata	•Not separate hazard ratios by event •Influenced by first event in injury setting
Inferences	Logical in multiple injury setting	Logical in multiple injury setting	•Limited usefulness in multiple injury setting •No event specific information
Largest PRO	Overall Simplicity	Easy comparisons between strata (injury events)	Could be useful in setting where risk factors for different event numbers were previously determined as the same
Largest CON	To compare injuries (events) may go to PWP	None	Limited usefulness when risk factors change by event number

In conclusion, the PWP Model appears to be the choice model for analysis of these data and perhaps more generally in settings where a single subject may experience multiple injuries. The assumptions inherent in this model are justifiable in the multiple injury setting. Additionally, this model is unlike the others as it allows for easy comparisons between the different strata (injury events). The Cox modelling approach will yield identical results to the PWP Model, however, it does not allow for easy comparisons between injury events. The AG Model is the most limited, primarily because the underlying assumptions do not correspond to the multiple injury setting.

APPENDIX

SAMPLE OF DATA

Data for Cox Model to First Event

ID	STATUS	TIME	AGE	ALCOHOL
700	1	69	27.8439	0
703	1	312	30.6119	1
704	0	396	22.1136	.
705	0	396	19.3320	0
707	0	396	33.6810	0
708	0	396	30.7187	1
709	0	396	24.9637	1
710	0	396	30.8939	0
711	0	396	28.3231	1
712	0	396	29.8316	1
714	0	396	23.0938	1

Data for Cox Model to Second Event

ID	STATUS	TIME	AGE	ALCOHOL
700	0	327	28.0329	0
703	0	84	31.4661	1

Data for PWP Model

ID	STATUS	TIME	STRATA	AGE		ALCOHOL	
				Str 1	Str 2	Str 1	Str 2
700	1	69	1	27.8439	0	0	0
703	1	312	1	30.6119	0	1	0
704	0	396	1	22.1136	0	.	0
705	0	396	1	19.3320	0	0	0
707	0	396	1	33.6810	0	0	0
708	0	396	1	30.7187	0	1	0
709	0	396	1	24.9637	0	1	0
710	0	396	1	30.8939	0	0	0
711	0	396	1	28.3231	0	1	0
712	0	396	1	29.8316	0	1	0
714	0	396	1	23.0938	0	1	0
700	0	327	2	0	28.0329	0	0
703	0	84	2	0	31.4661	0	1

Data for Andersen-Gill Model

ID	STATUS	TSTART	TSTOP	AGE	ALCOHOL
700	1	0	69	27.8439	0
700	0	69	396	27.8439	0
703	1	0	312	30.6119	1
703	0	312	396	30.6119	1
704	0	0	396	22.1136	.
705	0	0	396	19.3320	0
707	0	0	396	33.6810	0
708	0	0	396	30.7187	1
709	0	0	396	24.9637	1
710	0	0	396	30.8939	0
711	0	0	396	28.3231	1
712	0	0	396	29.8316	1
714	0	0	396	23.0938	1

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